CONTRIBUTIONS TO SURVIVAL MADE BY BODY CELLS OF GENETICALLY DIFFERENTIATED STRAINS OF MICE FOLLOWING X-IRRADIATIONS[1]

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Our strains of inbred mice have inherited relatively stable differences in their sensitivities to absorbed radiant energy (Gowen, 1950; Gowen and Zelle, 1945; Gowen and Stadler, 1956; Grahn, 1954) from whole-body irradiation. These differences are related to fixed variations in the normal cell structures of the strains (Gowen, 1945; Gowen and Calhoun, 1943; Gowen, 1952; Weir, 1949). Progress in understanding the mechanisms of irradiation damage may be advanced if genetic differences in resistance are traced to the cells as a whole or to particular organ systems. Regional body irradiation affords a technique for localizing organs significant to radiation resistance. This technique along with surgical removal and/or shielding before organ exposure has been tried with some indications that given organs are significant to irradiation resistance. Examination of irradiation effects on genetic strains of mice having known ranges in resistance combined with partial body exposure without confounding by surgical interference offers a promising means of attacking this problem.

Materials and Methods

The host constitutions in these experiments were differentiated into 5 distinct lines through 30 or more generations of brother-by-sister matings accompanied by selection for specific inherited types. The strains are homozygous albino but differ in coat color at the agouti locus. They are differentiated for resistance to *Salmonella typhimurium*, the typhoid-causing bacteria of mice. Under comparable conditions over a period of more than 20 years the mice of these strains maintain their relative resistances to 200,000 organisms to that observed in these experiments, S 100%, Z 45%, K 39%, Q 0% and Balb/Gw, hereafter called Ba, 0%. The strains differ genetically in body weight, growth rate, heart, kidney, liver, spleen and testis weights, serum globulins, leucocyte number, fixed phagocytic cells, macrophages, and cells metabolizing fat and storing glycogen as well as other significant physiological characteristics. The environment of the animals throughout the experimental period, as well as through many breeding generations, was that of a controlled laboratory where feed, water and management were uniform.

All mice were 46 ± 3 days of age at the time of irradiation. Strains and sexes were randomly distributed across the different treatments. Thirty-seven weeks

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were required to completely fill the experiment as designed. A General Electric Maxitron operated at 250 pkv, 30 ma with 0.25 mm. Cu + 1 mm. Al filtration at a distance of 47.5 cm. from anode to mid-mouse was used for the x-irradiation of all mice. The dose rate varied from 160 r/minute to 180 r/minute. Part of this range was accounted for by a change of x-ray tubes. Mice were held for x-irradiation in perforated plastic tubes with cork stoppers. These tubes were arranged in a wooden rack in two rows of eight tubes placed side by side with the closed ends of each row facing each other. The field of radiation covered by this rack of tubes permitted a range of only 12 r per minute over the entire area.

The experiment performed and analyzed was designed as a factorial having four elements. Five inbred strains of mice having known differences in x-ray and typhoid sensitivities were utilized in comparable numbers. The numbers for the two sexes were balanced for each strain. There were four x-ray exposure doses: 0, 320, 480 and 640 roentgens. The levels of x-ray dosage were chosen to span the range from no effect to nearly complete lethality when the mice were exposed to whole-body irradiation.

There were eight combinations of body coverage or exposure. The body of the mouse was divided into three regions—head, mid and rear. Shielding was with $\frac{1}{8}$ inch-thick strips of lead laid across the tubes covering the region or regions of the mice for a given treatment. The eight combinations of regions exposed are shown below.

Region Exposed

None
Head
Mid
Rear
Head-Mid
Head-Rear
Mid-Rear
Whole-Body

The head region or anterior third of the body extended into the thorax. The middle third of the body, mid region, included that part of the body containing lower thorax, and abdominal cavity containing stomach and upper intestinal tract, liver, spleen, adrenals, ovaries and kidneys. The posterior third of the body, rear region, included the lower intestinal tract, bladder, and urinary system and testes of the males. These regions are illustrated in Plate 1.

The eight groups of different regional exposures were treated with 320 r, 480 r and 640 r making a total of 24 different x-ray treatment groups. In addition the mice of one group were put in tubes and completely lead-covered for a time comparable to that of the longest dose, 640 r, but were not exposed. This group acted as a control on handling as well as for un-irradiated, 0 r group.

There were 25 treatment groups with 5 strains and 2 sexes making up 250 cells in the experiment. Each cell represented a different strain, sex, and treatment. A minimum of 25 mice were treated in each cell. Some cells contained a few extra animals. The completed experiment involved a total of 6904 mice.

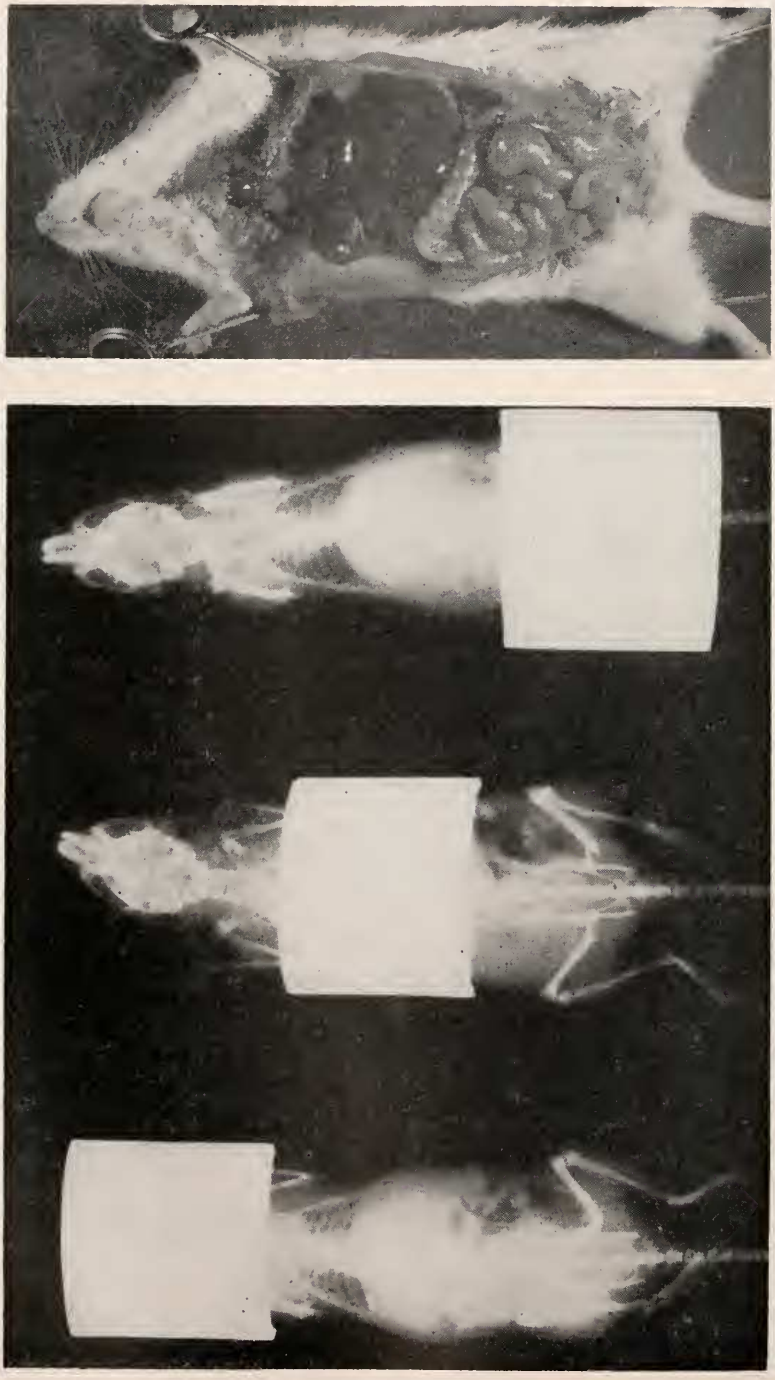

PLATE 1. Radiographs showing shielding marking off the three regions and their relation to the anatomy of the mouse.

The immediate effects of x-ray were largely completed 12 days following irradiation. Although there were marked differences in survival times between the different strains, few deaths occurred after the twelfth day. A 15-day interval following irradiation was allowed to cover the direct effects of exposure. Deaths were recorded daily and survivors of the fifteenth day were considered as surviving mice.

The ⅛-inch lead sheets used to delimit the body regions exposed to irradiation protected the shielded regions from the greater portion of irradiation. But this protection was not complete. The ⅛-inch lead was sufficient to absorb all but 0.75 r per minute. The back scattering of the radiation into the shielded regions accounted for larger doses of radiant energy in the protected regions. Measurements made when the tubes were placed on a nylon mesh screen under the same conditions showed that the back scattering largely came from the wooden rack used to hold the plastic tubes containing the mice. Only 7.4 r or 1.2 per cent of the 640 r dose was absorbed in the lead-covered mid-region when head and rear regions were exposed, whereas 78 r or 12.2 per cent of the x-rays was absorbed when the wooden rack was used. The amount of radiation absorbed in the different shielded regions varied from 3 to 12.2 per cent of the dose given. The region receiving most scattered radiation was the mid-region when the head and rear regions were exposed. This could be expected as the scattering could enter from two directions. The amount of radiation absorbed in any shielded region should tend to magnify somewhat the effects of the different treatments and reduce the differences between the treatments. The effects of scattered radiation were distributed through all treatment groups and tended to balance from one treatment to another. That this amount of radiation absorbed into the protected regions could lessen in some degree the recovery potentials of the mice treated in the region is recognized. The total roentgens scattered and absorbed should make this factor a minor contributor to the total variation.

The results of localizing radiation to particular regions of the body have been determined by comparison of sexes, strains and dosages across all regional exposure treatments in the factorially designed experiment. Two separate criteria have been used to measure the effects of irradiation, the percentage survival of the treated mice and the length of survival in days within the observational period.

Because of the unequal numbers of mice in the different treatment groups, all data have been analyzed throughout this paper by using disproportionate frequency analyses. Binomial analyses were used for the survival data and the customary methods for mean length of survival within the observational periods.

The data based on percentage survival did not allow for the full expression of the differences between strains, etc. Survival range had fixed limits at 0 and 100 per cent. These limits confined the quantitative estimates of the effects, *i.e.*, strain or radiation, to values within this range. Consequently all conclusions drawn from the percentage survival data led to minimal estimates by the nature of these limitations of the scale.

The data on length of survival were confined by one limiting measurement, the total length of the observation period. This fixed measurement again limited the full expression of the effects of irradiation on the mice. Any differences observed in both sets of data for each response were therefore minimal estimates of these consequences following the different treatments.

Experimental Results

The main purpose of this experiment was to examine the effects of irradiation to particular organs (body regions) and to their summation of effects on the cells of the body as a whole. Two variables are intrinsic in the data. Known genetic differences may assist in these analyses by introducing reliable differences in the resistance levels of the mouse strains. Sex of the mice utilized in the tests could affect the results although previous experience has shown that this is a minor factor in the expression of the mouse typhoid syndrome. The effects of sex and strain will be analyzed separately. The sex effects are considered first.

Effects of Sex

Irradiation may cause acute effects leading to death. In the range of x-ray exposures of this experiment these radiation deaths were largely over by 12 days post-irradiation. Consequences of the x-ray treatments were measured by percentages

Table I

Effect of sex on radiation sensitivity. Per cent survival in 15 days

Dose (r)	Region exposed	Mean per cent survived		Variance analyses			
				Within sex		Between sex 1 d.f.	
		Male	Female	d.f.	M.S.	M.S.	F
0	None	100	100	289	—	—	—
320	None	100	99	266	.004	.004	1.0
	Head	100	100	270	—	—	—
	Mid	100	99	267	.004	.004	1.0
	Rear	100	100	268	—	—	—
	Head-mid	99	100	270	.004	.004	1.0
	Head-rear	100	100	267	—	—	—
	Mid-rear	99	100	268	.007	.015	2.0
	Whole-body	97	95	271	.035	.019	0.5
480	None	98	100	257	.011	.034	3.0
	Head	100	100	258	—	—	—
	Mid	99	98	269	.018	.003	0.2
	Rear	100	100	265	—	—	—
	Head-mid	99	100	263	.004	.004	1.0
	Head-rear	100	100	269	—	—	—
	Mid-rear	99	100	276	.007	.015	2.1
	Whole-body	59	62	284	.241	.062	0.3
640	None	100	100	279	—	—	—
	Head	99	99	295	.010	.004	0.4
	Mid	97	97	286	.027	.000	—
	Rear	99	100	289	.003	.004	1.0
	Head-mid	92	95	284	.062	.092	1.5
	Head-rear	99	99	286	.010	.003	0.3
	Mid-rear	80	81	287	.159	.005	0.0
	Whole-body	7	3	271	.045	.090	2.0

TABLE II

Effect of sex on radiation sensitivity. Mean days survived in 15-day period

Dose (r)	Region exposed	Mean days survived		Variance analyses			
				Within sex		Between sex 1 d.f.	
		Male	Female	d.f.	M.S.	M.S.	F
0	None	15.0	15.0	289	—	—	—
320	None	15.0	15.0	266	0.06	0.06	1.0
	Head	15.0	15.0	270	—	—	—
	Mid	15.0	15.0	267	0.00	0.00	1.0
	Rear	15.0	15.0	268	—	—	—
	Head-mid	15.0	15.0	270	0.06	0.06	1.0
	Head-rear	15.0	15.0	267	—	—	—
	Mid-rear	14.9	15.0	268	0.15	0.30	2.0
	Whole-body	14.9	14.8	271	1.43	0.39	0.3
480	None	14.9	15.0	257	2.90	0.75	0.3
	Head	15.0	15.0	258	—	—	—
	Mid	14.9	14.8	269	1.20	1.02	0.9
	Rear	15.0	15.0	265	—	—	—
	Head-mid	15.0	15.0	263	0.14	0.13	1.0
	Head-rear	15.0	15.0	269	—	—	—
	Mid-rear	14.9	15.0	276	0.52	0.93	1.8
	Whole-body	13.6	13.8	284	5.02	1.91	0.4
640	None	15.0	15.0	279	—	—	—
	Head	14.9	14.9	295	0.38	0.06	0.2
	Mid	14.8	14.7	286	2.34	0.09	0.0
	Rear	14.9	15.0	289	0.28	0.28	1.0
	Head-mid	14.2	14.6	284	5.00	8.79	1.8
	Head-rear	15.0	15.0	286	0.06	0.03	0.5
	Mid-rear	13.2	13.3	287	14.18	0.42	0.0
	Whole-body	9.4	8.9	271	9.52	12.70	1.3

of the animals which survived for 15 days following exposure and by the average lengths of survival of the irradiated groups. The data are subdivided for each sex into the x-ray dose and the region of the body in which the mouse received the irradiation. The strains were nearly balanced in numbers and were combined in these tests.

Table I gives the data on the mice which survived the different x-ray treatments. The first column presents the x-ray dosage in air at the mid point of the mouse's body. Column 2 lists the body regions exposed to x-rays. Columns 3 and 4 give the mean survival as per cent of the mice surviving 15 days after the x-ray exposure according to the sex. The variance analyses give the degrees of freedom (d.f.) for the variances of the mice within sexes, the mean square (M.S.) between sexes with 1 d.f. and the F values for the mean squares. Throughout this paper * shows significance at the 0.05 level and ** at the 0.01 level.

Table I shows that only animals which received whole-body irradiation had appreciable mortality. In the 15-day period no mice died in the untreated group; the

320 r whole-body exposed mice showed a few scattered deaths, 3 and 5 per cent; the 480 r dose was more lethal, about 40 per cent of the mice died; and the 640 r dose was almost completely lethal, only 3 and 7 per cent survived of the 273 mice treated. Consideration of sex effects on radiation survival was consequently almost entirely limited to the 480 r and 640 r whole-body irradiation groups. The differences in responses of the sexes to irradiation were small throughout the 25 comparisons. In no case was a significant difference observed. The 480 r and 640 r whole-body exposures were severe enough to test any real biological changes in the physiologies of the sexes suffered through irradiation exposure. No sex differences appeared. In view of these facts the data for sexes have been combined in further consideration of these experiments on survival to x-radiation.

The severity of the x-ray effects may be measured by the number of days a mouse survives following x-ray exposure. Table II gives these data in the same form as Table I, with columns 3 and 4 showing the average number of days the males and females survived of the 15 days subsequent to x-irradiation. All treatment groups except the whole-body exposures at 320 r, 480 r and 640 r showed practically complete survival. The mean day survivals for whole-body exposures were 0 r—15 days, 320 r—14.9 days, 480 r—13.7 days and 640 r—9.1 days. The mean length of survival of the mice to whole-body irradiation was but slightly reduced by 320 r, was lowered by 480 r and was severely reduced by 640 r. The tests for sex effects on length of survival were only critical for the 480 r and 640 r whole-body irradiation groups. The sexes showed comparable mean days of survival. In no case was there a significant difference between sexes.

These results further support the conclusion that the sexes in mice are equally affected by x-irradiation. The conclusions on x-ray effects which are derived from these data will not be altered by combining the observations of the two sexes.

These tests also furnish a measure of the degree of protection afforded the animals by the coverage with lead plates. Animals of 0 r group were not exposed to x-rays but the bodies of the mice were completely shielded by ⅛-inch lead plates. The unexposed and 640 r groups had 100 per cent survival. In the 320 r treatment group exposed and lead-shielded, one female out of 268 animals died; the 480 r group had three males out of 259 mice die. Mortality at the three dose levels appeared fortuitous and unrelated to the irradiation. It was concluded that the protection with the lead shields was adequate for all groups.

Genetic Effects of Strains

The mice utilized in this experiment were known to exhibit differences in their abilities to withstand radiation. These differences have become isolated into different strains. The data on the genetic effects on resistance to radiation as evidenced by different strains within a treatment are presented in Table III.

Five treatments displayed strain effects on x-ray sensitivity. These exposures were: whole-body at 320 r and 480 r and mid, head-mid and mid-rear regions at 640 r. Examination of the mean strain survivals indicates that these differences came largely from the high susceptibility of the Ba strain. All strains were affected by the whole-body exposures, and the severity increased with dose. At 640 r the effects were so severe as to have overreached strain differences as judged by the F test, even though the strains still retained their relative order of resistance.

TABLE III

Genetic effects of strain differences on radiation sensitivity. Per cent survived 15 days post-irradiation

Dose (r)	Region exposed	Strains Per cent survival					Variance analyses			
							Within strains		Between strains 4 d.f.	
		S	Z	K	Q	Ba	d.f.	M.S.	M.S.	F
0	None	100	100	100	100	100	286	—	—	—
320	None	100	98	100	100	100	263	.004	0.004	1.1
	Head	100	100	100	100	100	267	—	—	—
	Mid	100	100	100	100	98	264	.004	0.004	1.0
	Rear	100	100	100	100	100	265	—	—	—
	Head-mid	100	100	98	100	100	267	.004	0.004	1.0
	Head-rear	100	100	100	100	100	264	—	—	—
	Mid-rear	100	100	100	100	97	265	.007	0.014	1.9
	Whole-body	98	100	94	100	90	268	.034	0.107	3.2*
480	None	100	100	96	100	98	254	.011	0.015	1.3
	Head	100	100	100	100	100	255	—	—	—
	Mid	98	100	98	98	97	266	.018	0.008	0.5
	Rear	100	100	100	100	100	262	—	—	—
	Head-mid	100	98	100	100	100	260	.004	0.004	1.0
	Head-rear	100	100	100	100	100	266	—	—	—
	Mid-rear	100	100	100	100	97	273	.007	0.013	1.9
	Whole-body	79	75	54	66	31	281	.213	2.116	9.9**
640	None	100	100	100	100	100	276	—	—	—
	Head	98	100	100	98	98	292	.010	0.005	0.5
	Mid	100	100	95	100	92	283	.026	0.082	3.1*
	Rear	100	100	100	100	98	286	.003	0.003	1.0
	Head-mid	98	98	96	100	75	281	.054	0.633	11.7**
	Head-rear	100	100	98	98	98	283	.010	0.006	0.5
	Mid-rear	92	96	71	98	49	284	.124	2.624	21.1**
	Whole-body	11	4	4	6	0	268	.045	0.085	1.9

Strain differences were separated most clearly when the animals were exposed to the 640 r. These strain differences appeared in all treatments. The 480 r treated mice showed the strain effects only in the whole-body irradiated class. The 320 r treated groups were at the border line where a reduction in survival was only beginning to appear in the whole-body treated mice of the most susceptible strain. The whole-body 480 r irradiations ordered the strains for resistance; the S was most resistant followed in order by the Z, Q, K and the most susceptible Ba.

In the 640 r dose range S, Z and Q strains were not very different in their responses. The Ba strain again showed the greatest radiation sensitivity with the K strain somewhat less sensitive than the Ba and noticeably less resistant than the other three strains.

The mean days of survival for the 15-day interval following irradiation and the analyses of the strain differences are presented in Table IV.

Table IV confirms the major features of Table III. Strain differences in resistance to irradiation were brought out in the 480 r whole-body treatment and with 640 r exposure when the mid, head-mid, mid-rear and whole body were treated. The significance tests identify a difference in radiation effects which made the two measures, per cent survival and length of survival, desirable. The 320 r whole-body exposure was sufficient to make the strain differences in per cent survival significant, whereas the mean length of survival did not show such differences. The mice that died, died late in the 15-day observation period. Following 640 r whole-body exposure, the mice showed only an insignificant difference in strain survivals even though all survival values were markedly reduced, whereas in length of survival the strain differences were accentuated to give a highly significant F value. The other three treatments, the mid, head-mid and mid-rear regions, suggest the mid region as the most sensitive to radiation damage.

TABLE IV

Genetic effects of strain differences on radiation sensitivity. Mean days survived in 15 days

Dose (r)	Region exposed	Strains Mean days survived					Variance analyses			
							Within strains		Between strains	
		S	Z	K	Q	Ba	d.f.	M.S.	M.S.	F
0	None	15.0	15.0	15.0	15.0	15.0	286	—	—	—
320	None	15.0	14.9	15.0	15.0	15.0	263	0.06	0.07	1.1
	Head	15.0	15.0	15.0	15.0	15.0	267	—	—	—
	Mid	15.0	15.0	15.0	15.0	15.0	264	0.00	0.00	1.0
	Rear	15.0	15.0	15.0	15.0	15.0	265	—	—	—
	Head-mid	15.0	15.0	14.9	15.0	15.0	267	0.06	0.06	1.0
	Head-rear	15.0	15.0	15.0	15.0	15.0	264	—	—	—
	Mid-rear	15.0	15.0	15.0	15.0	14.8	265	0.15	0.28	1.9
	Whole-body	14.8	15.0	14.9	15.0	14.5	268	1.41	2.30	1.6
480	None	15.0	15.0	14.8	15.0	15.0	254	0.29	0.52	1.8
	Head	15.0	15.0	15.0	15.0	15.0	255	—	—	—
	Mid	14.9	15.0	14.8	15.0	14.7	266	1.20	0.91	0.8
	Rear	15.0	15.0	15.0	15.0	15.0	262	—	—	—
	Head-mid	15.0	14.9	15.0	15.0	15.0	260	0.14	0.15	1.1
	Head-rear	15.0	15.0	15.0	15.0	15.0	266	—	—	—
	Mid-rear	15.0	15.0	15.0	15.0	14.7	273	0.52	0.84	1.6
	Whole-body	14.4	14.2	13.4	14.2	12.2	281	4.44	45.52	10.3**
640	None	15.0	15.0	15.0	15.0	15.0	276	—	—	—
	Head	14.9	15.0	15.0	14.9	14.9	292	0.38	0.20	0.5
	Mid	15.0	15.0	14.6	15.0	14.3	283	2.26	6.81	3.0*
	Rear	15.0	15.0	15.0	15.0	14.9	286	0.28	0.26	1.0
	Head-mid	14.9	14.8	14.8	15.0	12.8	281	4.32	53.74	12.4**
	Head-rear	15.0	15.0	15.0	15.0	15.0	283	0.06	0.03	0.5
	Mid-rear	14.4	14.7	12.4	14.8	10.2	284	11.01	235.54	21.4**
	Whole-body	10.6	10.4	8.8	10.4	5.4	268	5.72	265.42	46.4**

TABLE V

Effects of x-ray dosage to different body regions on survival 15 days after irradiation

Region exposed	Variance analyses							
	Doses 3 d.f.		Strains 4 d.f.		Dose×Strain 12 d.f.		Within dose and strain	
	M.S.	F	M.S.	F	M.S.	F	d.f.	M.S.
Percentage survival for 15 days post-irradiation								
None	No analysis—Practically all survived							
Head	No analysis—Practically all survived							
Mid	.048	3.9**	.044	3.6**	.017	1.4	1099	.012
Rear	No analysis—Practically all survived							
Head-mid	.291	18.6**	.156	10.0**	.162	10.3**	1094	.016
Head-rear	No analysis—Practically all survived							
Mid-rear	2.66	75.3**	.873	24.7**	.593	16.8**	1108	.035
Whole-body	54.00	734.9**	.869	11.8**	.480	6.5**	1104	.074
Mean days survived in 15 day post irradiation period								
None	No analysis—Practically all survived							
Head	No analysis—Practically all survived							
Mid	4.08	4.7**	3.27	3.7**	1.49	1.7	1099	.88
Rear	No analysis—Practically all survived							
Head-mid	22.12	19.1**	13.56	11.7**	13.46	11.6**	1094	1.16
Head-rear	No analysis—Practically all survived							
Mid-rear	220.15	73.7**	72.83	28.4**	54.61	18.3**	1108	2.99
Whole-body	2078.36	726.7**	131.31	45.9**	60.64	21.2**	1104	2.86

The mean days of survival of the five strains for the 25 different treatments showed somewhat less differentiation in the reactions of the strains to x-irradiation. The head-mid-rear exposure to 640 r showed the widest separation between Ba and K and these from the other three, S, Z, and Q strains. The order of the strains in resistance to radiation effects did not correspond to the order of these same strains in their natural resistance to mouse typhoid as noted earlier.

REGIONAL EFFECTS OF IRRADIATIONS AND GENOTYPES

Three elements were operating on the survival of the mice in this experiment, dosage of the x-rays, the region of the body exposed to x-rays and genotype as represented by strain of mice under treatment. Table V measures these effects first in terms of the mice surviving for 15 days following irradiation and second, the lower half of the table, in terms of mean length of survival within the 15-day period.

The data of Table V are presented for the body regions exposed, eight different categories in all. Of the eight groups four have not been analyzed as the deaths within these groups were few and scattered.

When the mid region only was exposed to x-rays, differences in dosage and in strains were evident and of equal significance. The dosage × strain interaction

was minor. Interaction between dosage × strain was a factor in survival when radiations were absorbed in the head-mid portion of the body. Both dosage and strain effects were large, with the dosage effects nearly double those of the strains. The interaction, however, was as large as the strain effects, indicating that the strains reacted differently to the different exposures.

X-rays to the rear two-thirds of the body gave even more noticeable effects. The effects of the dosages were markedly greater than the strain differences and the strain effects showed more than random deaths. The whole-body irradiations, those involving the head, mid and rear regions, were more severe than those of other treatments. The x-ray effects were so pronounced at the 640 r level (Table III) that they overshadowed the strain differences. The strain effects were clearer in the 480 r and 320 r whole-body treatment groups.

The data on length of survival within the 15-day interval following irradiation show essentially the same features as those for survival. Irradiation to the head-mid portion of the body was not as effective as that to the mid-rear portion, but both showed more change than when the x-rays were directed to the mid region alone. The mid region was sensitive but added irradiation to the rear or head regions increased the sensitivity. Irradiation to all regions leaves the body with no unexposed tissue. Under these conditions the survival values were materially reduced over those of all other types of treatment.

Quantitative Analyses of Regional Effects of X-ray Exposure

Quantitative estimates of the relative sensitivities of the different body regions were obtained by relating the survival values within the x-ray dosages for the different treatments. The basic theory was as follows.

A factor common to mice of each strain was assumed to represent the natural resistance of the strain. This factor was considered as alone responsible for the survival values attained by the unexposed control groups. It was common to mice of all groups before treatment and was in a sense the potential resistance of the strain against which the x-ray or other treatments operated to reduce viability. The factor was designated a. Irradiation to the head region contributed a factor, h, to extend or reduce life. Its value depended upon the dosage of radiation to the head but within any one dosage its effect was regarded as a constant. In the same manner irradiation effects to the mid region were regarded as due to a factor, m, and those to the rear region were considered due to a factor, r. When two regions were irradiated the effects of radiation were assumed to be additive, *i.e.*, $h + m$ for total effects of irradiation to the head-mid regions. Any unexposed cells within the body would contribute possibilities of continuing normal functions. Even a small fraction of the cells having normal functions might be of vital importance to the mouse. In consequence it was assumed that when the whole body was irradiated there were effects above and beyond those of $h + m + r$. These effects were represented by d. The full effects of whole-body irradiations were viewed as due to $h + m + r + d$. The d factor measured the importance of even a fraction of the body cells being normal in function. A system of eight equations was available for the analysis of these effects as expressed in the eight regional body treatments.

$$a = \text{value of control, unexposed mice}$$
$$a + h = \text{value of control} + \text{head exposed}$$
$$a + m = \text{value of control} + \text{mid exposed}$$
$$a + r = \text{value of control} + \text{rear exposed}$$
$$a + h + m = \text{value of control} + \text{head and mid exposed}$$
$$a + h + r = \text{value of control} + \text{head and rear exposed}$$
$$a + m + r = \text{value of control} + \text{mid and rear exposed}$$
$$a + h + m + r + d = \text{value of control} + \text{whole body exposed}$$

The values for a, h, m, r and d were obtained from the system of five simultaneous equations derived from the above by the method of least squares. These simultaneous equations are presented below. The P values in the equations were obtained as the sums of the observed values. Wherever a given factor entered into the basic equations it contributed to the corresponding P, *i.e.*, P_1 = the sum of the constants for all eight, P_2 = the sum of four equations where h entered, etc.

$$P_1 = 8\,a + 4\,h + 4\,m + 4\,r + 1\,d$$
$$P_2 = 4\,a + 4\,h + 2\,m + 2\,r + 1\,d$$
$$P_3 = 4\,a + 2\,h + 4\,m + 2\,r + 1\,d$$
$$P_4 = 4\,a + 2\,h + 2\,m + 4\,r + 1\,d$$
$$P_5 = 1\,a + 1\,h + 1\,m + 1\,r + 1\,d$$

The general solution for each of the constants was as follows:

$$a = 1/8\ (5\,P_1 - 3\,P_2 - 3\,P_3 - 3\,P_4 + 4\,P_5)$$
$$h = 1/8\ (-3\,P_1 + 5\,P_2 + 1\,P_3 + 1\,P_4 - 4\,P_5)$$
$$m = 1/8\ (-3\,P_1 + 1\,P_2 + 5\,P_3 + 1\,P_4 - 4\,P_5)$$
$$r = 1/8\ (-3\,P_1 + 1\,P_2 + 1\,P_3 + 5\,P_4 - 4\,P_5)$$
$$d = 1/2\ (1\,P_1 - 1\,P_2 - 1\,P_3 - 1\,P_4 + 4\,P_5)$$

The constants for the effects of irradiation, as measured by percentage survival, for different intensities to the different regions are shown in Table VI. The constants fitted the observations well as shown by the variations accounted for by the five factors as against the residual variation left after the fits were made.

As expected the severity of the effects of the x-rays to the different regions increased as dosage increased. The 320 r dose was not severe enough to separate the effects of exposure to particular body regions. The whole-body treatment even at this level of exposure showed the reduction in survival, d, to be greater than can be accounted for by the additive effects of $h + m + r$; d may be thought of as representing the recovery potential when any unexposed cells were present within the animal's body.

In the 480 r dose range the separation of body regions by irradiation effects was clearer. The values of m confirmed the greater sensitivity of the mid region in lowering the survival rates of the mice following x-irradiation. The head and

TABLE VI

Effects of x-irradiation to particular body regions on percentage survival of 5 different strains of mice

Constant	Dose (r)	Strains					Average
		S	Z	K	Q	Ba	
a	320	100	100	100.23	100	99.99	100.04
	480	99.55	100.25	99.54	99.53	99.54	99.68
	640	100.83	100.69	103.04	100.03	106.84	102.29
h	320	0	0	−0.68	0	0.88	0.04
	480	0.45	−0.75	0.46	0.47	1.29	0.38
	640	.01	−0.25	2.96	−0.92	−1.51	0.06
m	320	0	0	−0.68	0	−1.76	−0.49
	480	−0.45	−0.75	−0.46	−0.47	−2.13	−0.85
	640	−3.29	−2.07	−13.40	−0.04	−29.23	−9.61
r	320	0	0	0.23	0	−0.87	−0.13
	480	0.45	0.25	0.46	0.47	−0.37	0.25
	640	−2.47	−1.13	−9.91	−0.98	−14.63	−5.82
d	320	−1.75	0	−4.65	0	−8.41	−2.96
	480	−21.05	−24.00	−45.90	−34.48	−67.30	−38.55
	640	−84.37	−93.59	−78.91	−92.53	−61.46	−82.17

Variations in survival accounted for by the constants

Dose	d.f.	Mean squares				
		S	Z	K	Q	Ba
320 r	acc. 5†	15,935	16,000	15,711	16,000	15,404
	res. 3††	0	0	1.7	0	1.0
480 r	acc. 5	15,175	15,045	14,512	14,783	13,923
	res. 3	0.5	0.5	0.6	0.6	1.5
640 r	acc. 5	13,574	13,784	12,547	13,783	11,004
	res. 3	9.8	1.5	73.4	1.1	196.0

† acc. = Variation accounted for by the different regions.
†† res. = Residual or unaccounted for variation.

rear regions appeared of almost equal resistance in the strains. With the two exceptions of the *h* in the Z strain and *r* in the Ba strain, the *h* and *r* values for the other four strains showed a slightly stimulatory effect on viability. When the whole body was exposed to the 480 r x-rays the effects attributable to *d* were very severe. Since the effects as measured by the *h*, *m* and *r* values were not extreme and were quite consistent in the five strains, the order in magnitude of the *d* values for the five strains represented the levels of resistance of the strains to x-irradiation. The S mice were most resistant followed by the Z, Q, K and Ba in that order.

The effects of irradiation were more marked in all regions when the exposure

dose was 640 r. Except in the Q strain irradiation to the mid region, *m,* resulted in the severest reaction. The *r* values showed the rear region to be intermediate in resistance to irradiation. The head region as measured by *h* was least sensitive. The *d* values again portrayed the severity of exposure to x-rays in the absence of any unexposed cells or organs. The order of the strains in resistance to irradiation as observed from the *d* values with 480 r exposure and to a lesser degree with 320 r was not followed by the 640 r dose. As the *h, m* or *r* effects became greater the values of the *d* effects were decreased due to the limited range in which these constants operate. In the Ba strain survival from radiation had full expression from 0 per cent survival from whole-body exposure to 100 per cent survival for the unirradiated controls. The sensitivity of the mid region accounted for 29 per cent of the mortality. The sensitivity of the rear region accounted for 15 per cent more and that of the head region only 1.5 per cent. The *d* effect contributed 61 per cent additional mortality and was restricted by the 0 limit for survival.

The variation left unaccounted for after fitting the five constants was practically negligible when compared with that accounted for. The increased, but still minor, variation observed for the Ba strain at the 640 r exposure can best be attributed to the limitations of the scale for death and survival.

A like analysis of the data on length of survival (Table VII) added a little information to that already gained (Table VI). The values for *d* were more consistent with the innate resistance levels of the strains than were those based on percentage survival because the scale of measurement was not so restricted. However, at the lower x-ray doses the length of survival did not give more information than the percentage data because most mice lived the full 15 days. The mid region was again most susceptible to the x-rays with the rear next. Irradiations to the head showed little effect.

Discussion

The analyses of these data showed that sex had only inconsequential acute effects on the response of mice to irradiation. This observation agrees with that of Abrams (1951) for whole-body irradiation. Kaplan and Brown (1952) also found like reactions of the sexes in an experiment involving 1700 mice when sexes were equally distributed across several x-ray doses and fractions of the doses. Sex differences may be greater when life span effects are considered.

Comparisons of the mice without regard to strain show that the lethal effects of the whole-body x-rays increase with increase in kilovoltage, the 600 r at 250 pkv and 0.25 Cu + 1 Al filter being about as lethal as 960 r at 100 pkv Coolidge tube without filters (Gowen and Stadler, 1956).

Differences between the responses of the five strains of mice to x-irradiation were evident. Strain differentiation depended upon the x-ray dose. The more susceptible strains, Ba and K, reacted to the lower dose, 320 r, which had no effect on the survival of the S, Z and Q strains. As the exposure was increased to 480 r and 640 r the five strains were more clearly separated in their resistance levels. After exposure of the whole body to 480 r, 79 per cent of the S mice survived with a mean of 14.4 days. They were followed in order by Z, 75 per cent, 14.2 days; Q, 66 per cent, 14.2 days; K, 54 per cent, 13.4 days and Ba, 31 per cent with 12.2 days survival. The higher x-ray exposure of 640 r (250 kvp) delivered to the

TABLE VII

Effects of x-irradiation on body regions as measured by length of survival

Constant	Dose (r)	Strains					Average
		S	Z	K	Q	Ba	
a	320	15.00	15.00	15.01	15.00	15.00	15.00
	480	14.96	15.02	14.95	14.99	14.95	14.97
	640	15.06	15.06	15.24	15.01	15.64	15.20
h	320	0	0	−0.03	0.0	0.02	0.00
	480	0.03	−0.04	0.05	0.01	0.11	0.03
	640	0.01	−0.03	0.34	−0.01	−0.06	0.05
m	320	0	0	−0.03	0	−0.06	−0.02
	480	−0.03	−0.04	−0.05	−0.01	−0.18	−0.06
	640	−0.24	−0.18	−1.15	−0.06	−2.74	−0.87
r	320	0	0	0.01	0	−0.05	−0.01
	480	0.03	0.01	0.05	0.01	−0.02	0.02
	640	−0.19	−0.08	−0.84	−0.08	−1.36	−0.49
d	320	−0.21	0	−0.11	0	−0.41	−0.15
	480	−0.60	−0.73	−1.56	−0.83	−2.62	−1.27
	640	−4.03	−4.32	−4.76	−4.50	−6.04	−5.53

Variations in survival accounted for by the constants

Dose	d.f.	Mean squares				
		S	Z	K	Q	Ba
320 r	acc. 5†	360	360	359	360.0	356.
	res. 3††	0	0	0	0	.00
480 r	acc. 5	356	355	350	355	341.
	res. 3	0	0	.01	0	.01
640 r	acc. 5	333	334	312	335	277.
	res. 3	.06	.01	.61	.00	1.80

† acc. = Variation accounted for by the different regions.
†† res. = Residual or unaccounted for variation.

whole body was severe enough to appreciably narrow the range between the two extreme strains, S and Ba. The Z and Q strains interchanged positions in rank of resistance as measured by percentage survival, but were equal when the degree of severity was measured by length of survival. The strain differences were expressed only in the treatment groups where the radiation was of sufficient intensity to reduce survival of the more sensitive strains (Tables III and IV). The strains responded differently to the graded x-ray doses as shown in Table V. The interactions between x-ray doses and strains in the exposure treatment groups were about equal to the effects of the strains alone. Each strain appeared to have a reaction curve of its own.

This genetic differentiation of the strains in their response to radiation has been expanded by more recent observations on the LD50 values for 15 days under the same conditions of x-irradiation. The actual x-ray doses required to reduce survival of each strain 50 per cent were determined by exposing mice of different strains to a range of x-ray doses. The LD50 values obtained experimentally for whole body irradiations were S, 537 r; Q, 528 r; Z, 522 r; K, 481 r and Ba 438 r. From this information the Q and Z strains were more nearly alike in radiation sensitivity than was indicated in the 480 r whole-body treatment group of the experiment under discussion, but comparable to the levels determined by the 640 r exposure.

The genetic differentiation of these five strains of mice in their resistance to x-irradiation confirms the observations of Gowen and Zelle (1945) on some of these same strains and by Henshaw (1944b) on other strains. Henshaw found that C_3H mice were more sensitive than LAF_1 mice to whole-body irradiation as measured by survival and the effects on the blood picture. Kaplan and Paull (1952) showed differences between strains A and C57 black to radiation response. Differences between four strains were shown by Reinhard *et al.* (1954) with minimal lethal doses of x-irradiation. The four strains ranged in MLD values from 570 r for the Marsh strain to 492 r for C_3H. Grahn (1954), in this laboratory, observed genetic differences between six strains of mice (including S, Z and Ba) in radiation response as related to body weight changes. With respect to dosage relationships these observations are in agreement with the findings of many other investigators. Heineke (1905) reported that increased x-ray exposure reduced the efficiency of the blood-forming organs in mice. Lawrence and Tennant (1937) concluded that length of life of Swiss mice following x-irradiation was directly related to the dose given. As dose was increased they noted the increased frequency of diarrhea in the mice. Like conclusions were reported by Osborne *et al.* (1952) and by Kaplan and Brown (1952). This latter work involved adequate samples of mice for each of nine x-ray doses, 283 r to 1131 r, given in single exposures and in fractions of these total doses. From the single exposures mortality increased from 4 per cent at 283 r to 83 per cent at the 566 r dose level.

In this work the S, Z, K and Ba strains maintained the same order in both radiation response and in subsequent response to mouse typhoid. This experiment introduces a new strain, Q. The Q strain showed a difference in its reactions. It was quite resistant to x-rays but extremely susceptible to mouse typhoid. Q mice did not fit in the observed pattern of the other mice with respect to the two responses. The leucocyte level for the Q strain has not been determined but is of real interest. The level of the white blood count of this strain would be indicative of the causal relationship of leucocytes to disease resistance (Weir *et al.*, 1953; Gowen and Calhoun, 1943) or to radiation sensitivity (Gowen, 1952). The K strain, not included in the six strains previously tested, followed in line with the other strains in both disease resistance and numbers of leucocytes (Thompson, 1952).

Differences in regional sensitivities to x-rays became evident when the body regions and combinations thereof were irradiated. The order of increasing sensitivity was head, rear, head-rear, mid, head-mid, mid-rear and head-mid-rear or whole-body. The dosages were not adequate to appreciably affect survival when the head, rear or head-rear were x-rayed. Only those four groups in which the

mid third was involved gave noticeable differences for the strains and dosages. Comparison of the mid-rear to the head-mid indicated a greater radiation sensitivity of the rear third as contrasted with the anterior third of the body. The reduction in survival and length of survival was between four and five times as severe following exposure of the head-mid as it was following that of the mid alone. The mid-rear reaction was around 16 times as severe as that of the mid alone. The increased reduction was affected by the particular regions rather than by the proportion of the body exposed.

Although no attempt was made in this investigation to associate specific organs to radiation sensitivity, specific organs or tissues were implicated by their inclusion within a given region as shown in Plate 1. The posterior third of the body implied the intestines, testes, bladder, etc., whereas the mid portion included the spleen, liver, etc. Our observations on the sensitivity of the mid-rear region in part confirmed those of Warren and Whipple (1922). They found in dogs that the abdomens, comparable to the rear plus a good portion of the mid region in these data, were more sensitive to x-irradiation than the head and thoracic region. They attributed this increase in mortality from x-rays to severe toxemia and septicemia enhanced by exposure of the intestines. Bond *et al.* (1954) arrived at similar conclusions. Chrom (1935) separated the effects of exposure to the rear region from those to the rest of the abdomen. He concluded that the rear region, including the intestines, was not as sensitive as the upper part of the abdomen. These data also supported the conclusion of Osborne *et al.* (1952) that bacteremia and intestinal damage were not closely correlated. The observations of these investigators were supported by those which have been derived from our studies.

The greater sensitivity of the mid region as shown in our data may be related to the response of the lymphoid tissues, spleen and nodes. Heineke's (1905) observations, supported by those of Läwen (1909), showed the blood and blood-forming tissues to react strongly to x-radiation in rats, rabbits, mice and guinea pigs. Further emphasis on the hematopoietic tissues in radiation response as well as in recovery comes from the investigations of Lawrence and Tennant (1937), Ellinger (1945), Henshaw (1944a, 1944b, 1944c), Bloom and Jacobson (1948) and Barrow and Tullis (1952) to name but a few. Again the data of this paper may be interpreted as indicating the significance of the proper functioning of these organs as they affect survival.

The important role of the spleen, a center of hematopoiesis, has been demonstrated by the increased survival obtained by shielding this organ from x-radiation (Jacobson, 1954; Wissler *et al.*, 1953; and Bond *et al.*, 1950) and by the partial protection afforded irradiated animals by injections of splenic or bone marrow tissue homogenates (Jacobson, 1954; Cole and Ellis, 1953; Lorenz *et al.*, 1952; and Barnes and Loutit, 1955). Again the behavior of these organs under irradiation has parallel significance to the data on x-ray survival presented in this paper.

The quantitative interpretation of these data is, however, somewhat different. The authors cited above have tended to consider each organ studied as all-important to irradiation survival. Our data show that while the different regions were significant, their effects on survival were less impressive than these other investigators suggested.

The fitting of constants to the regional body effects offers a new approach to the evaluation of radiation effects to different regions of the body. This quantitative

estimation of regional effects confirms our previous observations that exposure of the head region or anterior third of the body is less effective in reducing survival than either of the other regions. X-ray doses in the range used did not appear to influence this minor effect. Exposure of the rear region was shown to be detrimental to survival at the higher exposure level of 640 r. This effect was consistent in the five strains although of minor importance to the Q strain. Irradiation to the mid region showed the greatest consistent reduction in survival for all strains. Increase in dosage increased the severity of the reaction in the strains. Greater mortality was observed in the more susceptible strains, Ba and K. Only the Q mice showed a different reaction; exposures of the rear or head were nearly as detrimental as those to the mid region, although the effects of the three regions were small.

The greatest reduction in survival resulted from whole-body irradiation. The amount of this reduction as measured by the constant, *d,* was above that due to the combined effects of head, mid, and rear exposures. The *d* values represent that percentage of the total mortality that resulted when all cells of the body were exposed and is in addition to the mortality resulting from the combined exposures to the three portions of the body. The magnitudes of these *d* values particularly after 640 r, but also after 480 r, indicate the importance of at least some unexposed cells in facilitating the recovery of the irradiated animal. The large differences between the combined effects of the three regions as compared to the body irradiation, *d,* suggest that any unexposed cells contribute materially to the protection of the mouse from irradiation. This was also indicated by the work of Gershon-Cohen *et al.* (1951), who showed that shielding areas comparable to 15 per cent of the total body area of mice resulted in reduced mortality from radiation. Almost equal protection was afforded the mice by shielding the liver, or lung or abdomen. They concluded that viability of the animal was increased by shielding any part of the hematopoietic system and was not confined to special organs. Jacobson *et al.* (1951) compared the hematopoietic recovery in mice irradiated with regions or organs shielded from exposure to 1025 r. Shielding of the spleen gave the greatest increase in survival as well as in hematopoietic recovery. Shielding of the liver lobe or portion of the intestines increased survival, but to a lesser degree. These results were associated with only somewhat less recovery of hematopoiesis. However, shielding of the head gave nearly the same increase in survival as that of the intestine, but recovery in blood formation was only partial. The protection of the right hind limb, but not of the kidney, was also beneficial to survival. The results from the head and intestine shielding point to the influence of cells, tissues or systems, other than those involved in hematopoiesis, as contributing to the radiation response. Although injections of suspensions of splenic tissues contributed most, bone marrow and liver tissues as well as body tissues of embryos contributed to recovery of the irradiated host (Jacobson *et al.,* 1955). Our own observations do not rule out a major role for the hematopoietic system, but the increased severity of radiation to the whole body over that to the regions suggests that any cells, regardless of their apparent morphological specificity, could stimulate recovery. The scattered radiation absorbed in the shielded regions would tend to increase the effects to the exposed regions. Consequently the presence of scattered radiation would tend to decrease the *d* value as obtained here (Table VI).

In all cases the Ba mice show the largest effects of the regional exposures; the

d values have been minimized, however, by the limitation of 0 per cent survival. The K strain as previously shown is next in susceptibility to radiation followed by the Q, Z and S strains. The resistance of the S strain appeared related to the resistance of its cells to better withstand radiation even though exposures to the mid and rear regions were more detrimental to survival of the S mice than to the Z or Q mice. The resistances of the Z and Q strains appeared to be determined by the interactions of all cells and regions. The increased susceptibility of the K and Ba strains was contributed to by the proportionately greater sensitivity of the mid and rear regions. The five strains, however, showed quite similar reactions but to different degrees in their responses to x-irradiation. These results were in contrast to those of Reinhard *et al.* (1954). They found marked differences in four strains of mice in radiation sensitivity of the head as compared to that of the remainder of the body. Kaplan and Paull (1952) also showed strain differences between A and C57 black mice in the results of spleen shielding. Protection of the spleen was more important to A mice than to C_3H mice. This observation of the A strain was in accord with that of Lorenz *et al.* (1952). They observed differences between four strains of mice in their responses to the protection afforded by bone marrow cell suspensions. Intravenous and intraperitoneal injections of the homogenate increased survival for two strains, L and LAF_1. For strains A and C_3H intraperitoneal injections were of little value in decreasing mortality.

The data indicate the importance of maintaining at least some cells free of irradiation if the organism is to survive. The body cells retain a significant totipotency which contributes to maintaining the organism as a whole even though the cells may have differentiated to extreme types anatomically or physiologically.

Summary and Conclusions

1. The influence of x-irradiation absorbed in three body regions and in the combinations of these regions has been measured by three subsequent responses: survival to radiation, natural resistance to disease and ability to acquire resistance following contact with the disease agent, *S. typhimurium*. The effects of irradiation are presented in this paper. Papers on natural and acquired resistance will follow. The experiment was designed as a factorial with five genetically differentiated strains of mice, S, Z, K, Q and Ba; four levels of radiation: 0 r, 320 r, 480 r and 640 r; eight treatment groups and two sexes. All mice were 46 ± 3 days of age when irradiated from a 250 pkv x-ray source operated at 30 ma with 0.25 mm. Cu + 1 mm. Al filter at a dose rate averaging 170 r/minute. For the initial treatment the strains and sexes were well balanced, at least 50 mice in each of the 25 different treatment groups. The bodies of the mice were marked off in three regions, head *h,* mid *m,* and rear *r,* each comprising one-third of the body length. These regions, their combinations and their controls with each irradiation account for the 25 treatment groups. Shielding was done with $\frac{1}{8}$-inch lead. As most deaths occur between 7 and 12 days, an interval of 15 days was allowed for expression of any direct effects due to radiation. Deaths were recorded daily.

2. Percentage survival and length of survival were the two measurements used for determining the reactions in each response.

3. The sexes responded in like manner to x-irradiation. A penetration or wavelength effect was indicated in these data. The reactions of the mice to the whole

body irradiation at 250 pkv, 0.25 Cu + 1 Al filter 600 r were similar to those for 100 pkv, Coolidge tube, no filtration, 960 r.

4. Within the x-ray dose range used the responses of the strains to x-irradiation were shown to be partially genetically determined.

5. The levels of radiation resistance were in the order from resistant to sensitive: S, Z, Q, K and Ba. After 480 r total-body exposure the survival percentages of the five strains were: S, 79; Z, 75; Q, 66; K, 54 and Ba, 31. This order does not coincide with the order known to be followed in natural resistance to mouse typhoid: S, Z, K, Q and Ba.

6. Shielding of one-third of the body protected the mice of the five strains from 320 r and 480 r x-radiation, and to much lesser degree, depending upon regional exposures, from 640 r. The dose of 640 r was not of sufficient intensity to allow full expression of strain differences for the different regional exposures.

7. Whole-body exposure to 320 r reduced the 15-day survival for the more sensitive strains Ba and K, 480 r decreased survival in the five strains; 640 r was severe enough to largely overcome the genetic differences between the strains.

8. The mid region of the mouse was most sensitive of the three single regions, and more sensitive than the combined head and rear regions. The radiation effects were determined by the region rather than by the area of the body exposed.

9. The mid region in combination with the rear region showed greater sensitivity than the head-mid region. All strains were reduced in survival by exposure of the mid-rear to 640 r, whereas only the less resistant strains Ba and K showed the effects from the exposures of the less sensitive regions.

10. The decrease in survival showed the mid region as most sensitive for S, Z, K and Ba, followed by the rear portion with the anterior third of the body resistant. These four strains responded in the same manner but to different degrees.

11. The reactions of the Q strain separated it from the four other strains. Its level of radiation resistance with respect to the other strains was in contrast to its low level of natural resistance to mouse typhoid. Radiation resistance and natural resistance to this disease have been found highly correlated in seven of our strains of mice. The Q mice show comparable though slight sensitivity to x-radiation in the three body regions. Mortality in the Q strain was largely confined to whole-body exposures of 480 r and 640 r. This suggests that the Q mice have no particular center of radiation sensitivity, but that mortality is the result of the interactions of the cells throughout the body.

12. The data on length of survival confirmed the results from percentage survival and contributed additional information for those reactions that resulted in 0 or near 0 per cent survival.

13. The lead shielding, ⅛-inch in thickness, was adequate to protect the given regions from radiation. The three groups completely shielded when exposed to the three dosages of x-rays did not quite duplicate the 0 r group in their reactions. Mortality appeared unrelated to the x-ray dose, as 100 per cent survived 640 r, 98.4 per cent the 480 r and 99.6 per cent the 320 r.

14. The strains exhibited their own characteristic responses to different x-ray doses as was evidenced by the large values for dosage × strain interactions. These interactions were real, representing the expressions of genetic resistance and as such would contribute to the strain effects.

15. The effects of the relative sensitivities of the body regions were estimated quantitatively as well as qualitatively. The quantitative estimates compared favorably with the qualitative observations.

16. The additivity of the regional effects is supported by the little unaccounted-for variation remaining after fitting the constants derived on the assumption that *h, m, r* and *d* were additive in effect.

17. Mortality from whole-body irradiation was only partially accounted for by the combined mortalities resulting from the exposures to the different regions of the body. The effect of total-body exposure over and beyond that of the combined regional effects, *d,* was interpreted as a measure of the reaction when all cells of the body of the mouse had been exposed, or when all recovery potential had been affected.

18. The whole-body effect, *d,* was large and suggested that all cells may contribute to recovery regardless of the organ or system involved. As a consequence, protection of any cells of the body during exposure to radiant energy may stimulate recovery.

19. In terms of host resistance the unexposed cells over-compensate. The extreme over-compensation initiated by cells in different unexposed regions when cells of other regions are inactivated points to the significance of all body cells in resistance whatever their degree of tissue or organ differentiation.

20. These results indicate that the body cells retained a totipotency to assist in maintaining the organism as a whole despite the differentiation which these cells may have undergone since their stem cells left the embryologically differentiating primitive tract. They further show the importance of maintaining at least a small portion of the body free from irradiation if irradiation exposure should occur through accident or calculated risk.

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